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=> d his ful

(FILE 'HOME' ENTERED AT 19:25:41 ON 31 OCT 2002)

FILE 'REGISTRY' ENTERED AT 19:25:48 ON 31 OCT 2002

L1 36414 SEA GALLIUM  
L2 1 SEA GALLIUM/CN  
L3 0 SEA GALLIUM AND HYDROXY AND PYRONE  
L4 0 SEA GALLIUM AND HYDROXY? AND PYRONE?  
L5 2520 SEA GALLIUM COMPLEX  
L6 0 SEA L5 AND PYRONE  
L7 0 SEA HYDROXYPYRONE AND GALLIUM  
L8 1 SEA HYDROXYPYRONE  
D  
L9 0 SEA GALLIUM AND PYRANONE  
L10 50 SEA GALLIUM AND PYRAN?  
D 1-50  
L11 1 SEA GALLIUM NITRATE/CN  
D  
L12 1 SEA DIDEOXYINOSINE/CN  
L13 1 SEA DIDEOXYCYTIDINE/CN  
L14 0 SEA 5-AZIDOTHEMIDINE/CN  
L15 0 SEA 5-AZIDOTHYIMIDINE/CN  
L16 2 SEA AZT/CN  
D  
D 2

FILE 'REGISTRY' ENTERED AT 19:31:40 ON 31 OCT 2002

L17 1 SEA 30516-87-1/RN  
D L17 SQIDE TOTAL

FILE 'EMBASE, BIOSIS, EUROPATFULL, JAPIO, ADISALERTS, ADISINSIGHT,  
ADISNEWS, BABS, BIOBUSINESS, BIOCOMMERCE, BIOTECHNO, CANCERLIT, CAPLUS,  
CBNB, CEN, CIN, CONFSCI, DGENE, DIOGENES, DRUGB, DRUGLAUNCH, DRUGMONOG2,  
DRUGNL, DRUGU, DRUGUPDATES, EMBAL, ESBIODBASE, ...' ENTERED AT 19:32:09

ON

31 OCT 2002

L18 112 SEA 5-AZT  
L19 35 SEA 5-AZIDOTHYIMIDINE  
D 1-35 KWIC  
D 29

FILE 'REGISTRY' ENTERED AT 19:35:10 ON 31 OCT 2002

L20 0 SEA 5-AZT  
L21 5021 SEA 5 AZIDO?  
L22 0 SEA 5 AZIDOTHYIMIDINE  
L23 7 SEA AZIDOTHYIMIDINE  
D 1-7

FILE 'EMBASE, BIOSIS, EUROPATFULL, JAPIO, ADISALERTS, ADISINSIGHT,  
ADISNEWS, BABS, BIOBUSINESS, BIOCOMMERCE, BIOTECHNO, CANCERLIT, CAPLUS,  
CBNB, CEN, CIN, CONFSCI, DGENE, DIOGENES, DRUGB, DRUGLAUNCH, DRUGMONOG2,  
DRUGNL, DRUGU, DRUGUPDATES, EMBAL, ESBIODBASE, ...' ENTERED AT 19:36:46

ON

31 OCT 2002

L\*\*\* DEL 75 DUP REM L18 (37 DUPLICATES REMOVED)  
D 1- KWIC

L\*\*\* DEL 1476 S (GALLIUM OR L2 OR L10 OR L11) AND (HIV OR HUMAN IMMUNO?  
VIR?

L\*\*\* DEL 791 S L25 AND HIV

L\*\*\* DEL 599 DUP REM L26 (192 DUPLICATES REMOVED)

L\*\*\* DEL 65 S L26 AND (RIBO? (A) REDUCTAS?)

L\*\*\* DEL 7 S L28 AND HIV-2  
D 1-7  
D 7 KWIC  
D 6 KWIC

L\*\*\* DEL 28 S L26 AND HIV-2  
D 1-28  
D 27 KWIC  
D L28 1-65

L\*\*\* DEL 513 S L26 NOT (L28 OR HIV-2)  
D 1-513  
D 504 KWIC  
D 307 KWIC  
D 199 KWIC  
D 188 IALL  
D 187 IALL  
D 185 IALL  
D 184 IALL  
D 146 IALL  
D 108 IALL  
D 61 IALL

L\*\*\* DEL 685 S L25 NOT L26

L\*\*\* DEL 495 DUP REM L34 (190 DUPLICATES REMOVED)  
D 1-495

L24 236 SEA (GALLIUM OR L2 OR L10 OR L11) AND (RIBO? OR RNA) (5A)  
(REDUCT?)

L25 0 SEA L24 AND NEUCLEOSID? (5A) INHIBIT?

L26 0 SEA (GALLIUM OR L2 OR L10 OR L11) AND (NEUCLEOSID?) (5A)  
(INHIBIT?)

L27 95 SEA (GALLIUM OR L2 OR L10 OR L11) AND (NUCLEOSID?) (5A)  
(INHIBIT?)

L28 93 DUP REM L27 (2 DUPLICATES REMOVED)  
D 1-93 KWIC

L29 133 DUP REM L24 (103 DUPLICATES REMOVED)

L30 72 SEA L29 NOT L27

L31 61 SEA L29 AND L27  
D 1-61

L32 72 DUP REM L30 (0 DUPLICATES REMOVED)  
D 1-72  
D 72 IALL  
D 68 IALL  
D 67 IALL  
D 49 IALL  
D 45 IALL

L33 60 SEA GALLIUM MALTOLATE OR 108560-70-9

L34 21 SEA L33 AND (AIDS OR HIV OR HUMAN IMMUNO?)

L35 18 DUP REM L34 (3 DUPLICATES REMOVED)  
D 1-18

d his ful

(FILE 'HOME' ENTERED AT 19:25:41 ON 31 OCT 2002)

FILE 'REGISTRY' ENTERED AT 19:25:48 ON 31 OCT 2002

L1 36414 SEA GALLIUM  
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L10 50 SEA GALLIUM AND PYRAN?  
D 1-50  
L11 1 SEA GALLIUM NITRATE/CN  
D  
L12 1 SEA DIDEOXYINOSINE/CN  
L13 1 SEA DIDEOXYCYTIDINE/CN  
L14 0 SEA 5-AZIDOTHEMIDINE/CN  
L15 0 SEA 5-AZIDOTHYIMIDINE/CN  
L16 2 SEA AZT/CN  
D  
D 2

FILE 'REGISTRY' ENTERED AT 19:31:40 ON 31 OCT 2002

L17 1 SEA 30516-87-1/RN  
D L17 SQIDE TOTAL

FILE 'EMBASE, BIOSIS, EUROPATFULL, JAPIO, ADISALERTS, ADISINSIGHT, ADISNEWS, BABS, BIOBUSINESS, BIOCOMMERCE, BIOTECHNO, CANCERLIT, CAPLUS, CBNB, CEN, CIN, CONFSCI, DGENE, DIOGENES, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, DRUGUPDATES, EMBAL, ESBIODASE, ...' ENTERED AT 19:32:09

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L18 112 SEA 5-AZT  
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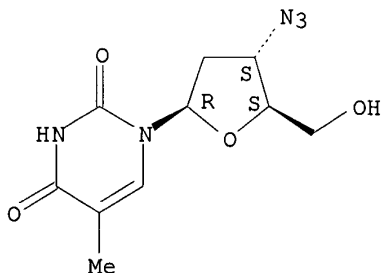
ON

31 OCT 2002

L24 75 DUP REM L18 (37 DUPLICATES REMOVED)  
 D 1- KWIC  
 L25 1476 SEA (GALLIUM OR L2 OR L10 OR L11) AND (HIV OR HUMAN IMMUNO?  
 VIR? OR L12 OR DIDEOXYINOSINE OR L13 OR DIDEOXYCYTIDINE OR  
 INOSINE OR CYTIDINE OR THYMIDINE OR AZIDOTHYMIDINE OR AZT OR  
 L17)  
 L26 791 SEA L25 AND HIV  
 L27 599 DUP REM L26 (192 DUPLICATES REMOVED)  
 L28 65 SEA L27 AND (RIBO? (A) REDUCTAS?)  
 L29 7 SEA L28 AND HIV-2  
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 D 7 KWIC  
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 L30 28 SEA L27 AND HIV-2  
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 L31 513 SEA L27 NOT (L28 OR HIV-2)  
 D 1-513  
 D 504 KWIC  
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 D 199 KWIC  
 D 188 IALL  
 D 187 IALL  
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 D 184 IALL  
 D 146 IALL  
 D 108 IALL  
 D 61 IALL  
 L32 685 SEA L25 NOT L26  
 L33 495 DUP REM L32 (190 DUPLICATES REMOVED)  
 D 1-495

CN 874: PN: WO02055741 SEQID: 889 claimed sequence  
 CN **Azidothymidine**  
 CN Azitidin  
 CN AZT  
 CN AZT (pharmaceutical)  
 CN BW-A 509U  
 CN NSC 602670  
 CN Retrovir  
 CN Retrovir IV  
 CN Timazid  
 CN ZDV  
 CN Zidovudine  
 FS STEREOSEARCH  
 DR 399024-19-2  
 MF C10 H13 N5 O4  
 CI COM  
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS,  
 BIOSIS,  
 BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN,  
 CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHM, CSNB, DDFU, DIOGENES,  
 DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB\*, IFICDB, IFIPAT,  
 IFIUDB, IPA, MEDLINE, MRCK\*, MSDS-OHS, NIOSHTIC, PHAR, PHARMASEARCH,  
 PIRA, PROMT, RTECS\*, SPECINFO, SYNTHLINE, TOXCENTER, ULIDAT, USAN,  
 USPAT2, USPATFULL, VETU  
 (\*File contains numerically searchable property data)  
 Other Sources: DSL\*\*, WHO  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (+).



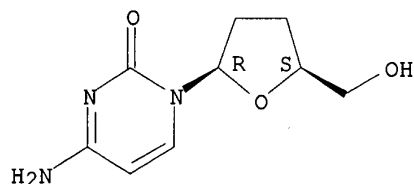
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4148 REFERENCES IN FILE CA (1962 TO DATE)  
 165 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 4157 REFERENCES IN FILE CAPLUS (1962 TO DATE)  
 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L40 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2002 ACS  
 RN 7481-89-2 REGISTRY  
 CN Cytidine, 2',3'-dideoxy- (8CI, 9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN 2',3'-Dideoxycytidine

CN 877: PN: WO02055741 SEQID: 892 claimed sequence  
 CN D 2C  
 CN ddC  
 CN **Dideoxycytidine**  
 CN Hivid  
 CN NSC 606170  
 CN PN: WO9948371 PAGE: 45 claimed sequence  
 CN Ro 24-2027/000  
 CN Zalcitabine  
 FS STEREOSEARCH  
 DR 176485-55-5  
 MF C9 H13 N3 O3  
 CI COM  
 LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*,  
 BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB,  
 CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU,  
 DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, IPA, MEDLINE,  
 MRCK\*, NIOSHTIC, PHAR, PROMT, RTECS\*, SPECINFO, TOXCENTER, ULIDAT,  
 USAN,  
 USPAT2, USPATFULL, VETU  
 (\*File contains numerically searchable property data)  
 Other Sources: DSL\*\*, WHO  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (+).

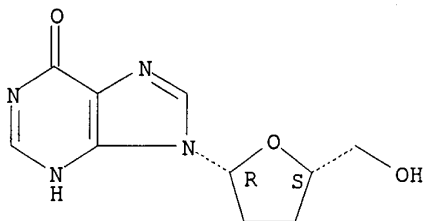


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1257 REFERENCES IN FILE CA (1962 TO DATE)  
 43 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 1264 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L40 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2002 ACS  
 RN 69655-05-6 REGISTRY  
 CN Inosine, 2',3'-dideoxy- (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN 2',3'-Dideoxyinosine  
 CN 876: PN: W002055741 SEQID: 891 claimed sequence  
 CN BMY 40900  
 CN DdI  
 CN DdI (nucleoside)  
 CN Didanosine  
 CN **Dideoxyinosine**  
 CN NSC 612049  
 CN Videx  
 FS STEREOSEARCH  
 MF C10 H12 N4 O3  
 CI COM  
 LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*,  
 BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT,  
 CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHM, CSNB, DDFU,  
 DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE, HSDB\*, IPA,  
 MEDLINE, MRCK\*, MSDS-OHS, PHAR, PROMT, RTECS\*, SYNTHLINE, TOXCENTER,  
 ULIDAT, USAN, USPAT2, USPATFULL, VETU  
 (\*File contains numerically searchable property data)  
 Other Sources: DSL\*\*  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1559 REFERENCES IN FILE CA (1962 TO DATE)  
 31 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 1568 REFERENCES IN FILE CAPLUS (1962 TO DATE)

L40 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2002 ACS  
 RN 30516-87-1 REGISTRY  
 CN Thymidine, 3'-azido-3'-deoxy- (7CI, 8CI, 9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN 3'-Azido-3'-deoxythymidine  
 CN 3'-Azidothymidine  
 CN 3'-Deoxy-3'-azidothymidine



L32 ANSWER 72 OF 72 FEDRIP COPYRIGHT 2002 NTIS

ACCESSION NUMBER: 2002:46310 FEDRIP

NUMBER OF REPORT: VA 129270

NUMBER OF CONTRACT: 0005, 584

RESEARCH TITLE: **Gallium** Therapy for Mycobacterial Infections

STAFF: Principal Investigator: Schlesinger, Larry S., M.D.  
PERFORMING ORGN: Department of Veterans Affairs, Medical Center, Iowa City, IA

SUPPORTING ORGN: Supported By: Department of Veterans Affairs, Research and Development (15), 810 Vermont Ave.

N.W.,

Washington, D.C., 20420, United States of America  
Sep 2, 1999

PROJECT START DATE:

FILE SEGMENT: Department of Veterans Affairs

SUMMARY: TUBERCULOSIS; RADIOTHERAPY; MYCOBACTERIUM INFECTIONS

OBJECTIVE: We propose the following two specific  
aims: 1) examine mechanism(s) whereby Ga is

acquired

and exhibits its microbicidal effects of M. tuberculosis (M.tb) and M. avium/intracellular complex (MAC), and 2) determine the mechanism(s) whereby Ga trafficks from the extracellular environment to the mycobacterial phagosome in macrophages and its effect on mycobacterial

viability

in this location. RESEARCH PLAN: **Gallium** (Ga), a group IIIA transition metal, particularly

in

the form of Ga nitrate [Ga(NO<sub>3</sub>)<sub>3</sub>], has been used clinically to localize neoplasms and inflammatory sites due to its concentration in tumor cells and macrophages and also to treat malignant neoplasms

and

associated hypercalcemia. The effects of Ga relate

to

its ability to substitute for Fe in many biomolecular processes, thereby disrupting them. Ga targets **ribonucleotide reductase** (RR) in eukaryotic cells, a critical enzyme in DNA replication. Bacteria also contain RR. Ga, like Fe, enters macrophages via both transferrin-dependent

and

transferrin-independent mechanisms. Thus, we hypothesize that Ga compounds may represent a new class of agents for treating mycobacterial

infections

through disruption of bacterial Fe-dependent metabolic pathways. Our goal is to characterize completely the mechanism of action of Ga against pathogenic mycobacterial with the eventual goal to determine the feasibility of the use of Ga compounds as therapeutic agents for this important group of pathogens. METHODOLOGY: Our methods include cell

culture, radiolabeled Ga binding studies and assays of enzyme activity. FINDINGS: Our studies indicate that Ga inhibits the growth of M.tb including an MDR strain, and MAC extracellularly and within human macrophages. Ga treatment is cidal against M.tb growing in macrophages. The Ga-mediated growth inhibition is additive with other anti mycobacterial drugs. The effect of Ga is reversed with excess Fe and Ga interrupts the ability of intracellular M.tb to acquire exogenous Fe. Finally, our studies indicate that Ga reduces the enzymatic activity of purified recombinant RR from M.tb. Our methods include cell culture, radiolabeled Ga binding studies and assays of enzyme activity. Recent studies show that Ga is effective against a range of iron and has activity in a guinea pig model of tuberculosis. CLINICAL RELEVANCE: Diseases due to M.tb and MAC cause significant worldwide morbidity and mortality especially in AIDS patients. MAC are uniformly multidrug-resistant (MDR) and MDR strains of M.tb are becoming more prevalent. Treatment requires multiple antibiotics with significant toxicity administered over months to years. Thus, there is the need to evaluate novel, effective therapeutic agents with the promise of reducing the duration of therapy. M.tb and MAC are representative of a group of intracellular pathogens that enter and multiply within mononuclear phagocytes. Iron (Fe) availability is critical for mycobacterial growth, making disruption of this aspect of mycobacterial metabolism an attractive target for antimicrobial therapy.

SUBJECT INDEX TERM: TUBERCULOSIS; RADIOTHERAPY; MYCOBACTERIUM INFECTIONS

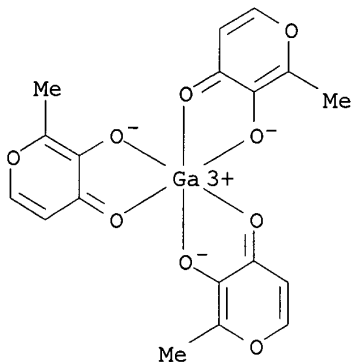
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L28 ANSWER 1 OF 65 DRUGNL COPYRIGHT 2002 IMSWORLD

ACCESSION NUMBER: 2001:1271 DRUGNL  
TITLE: **gallium** maltolate Titan phase change II, USA  
(cancer)  
SOURCE: R&D Focus Drug News (9 Apr 2001).  
WORD COUNT: 99

L28 ANSWER 2 OF 65 DRUGUPDATES COPYRIGHT 2002 IMSWORLD

ACCESSION NUMBER: 2000:750 DRUGUPDATES  
SOURCE: R&D Focus, (9 Apr 2001)  
GENERIC NAME: **gallium maltolate**  
CHEMICAL NAME: (OC-6-21)-tris[3-(hydroxy-kappaO)-2-methyl-4H-pyran-4-onato-kappaO4]gallium  
CAS REGISTRY NO.: 108560-70-9  
STRUCTURE:



CLASSIFICATION: L1X Other Cytostatics; J5C9 Other HIV Antivirals  
HIGHEST DEV. PHASE: Phase II (40)

COMPANY INFORMATION:  
Type |Company| Nationality  
=====+=====+=====  
Originator|Titan |United States  
-----+-----+-----  
Assignee |GeoMed |

L28 ANSWER 3 OF 65 PHAR COPYRIGHT 2002 PJB  
AN 26705 PHAR  
DN 031094  
CN **gallium** maltolate  
CN 4H-Pyran-4-one, 3-hydroxy-2-methyl-, **gallium** complex  
STA Active

CO

Type	Company Name (Country)	Development Status
Originator	Titan Pharmaceuticals (United States)	Phase II Clinical Trial

SO Pharmaprojects. PJB Publications Ltd., Richmond, Surrey, UK  
TX **Gallium** maltolate is an orally-active **ribonucleotide reductase** inhibitor, under development by Titan Pharmaceuticals for the treatment of cancer (Press release, Titan, 2 Apr 2001; Company Web Page, Titan, 25 Jan 2002).

#### Marketing

It was acquired by Titan when Titan acquired GeoMed (Press release, Titan, 20 Jul 2000).

#### Clinical

Phase III It is in a multicentre Phase II clinical trial in 104 patients with refractory multiple myeloma, metastatic prostate cancer, metastatic bladder cancer and refractory lymphoma. It will be administered at 1 of 3 dose levels in 28-day cycles to determine safety and tumour response (Press release, Titan, 2 Apr 2001; Direct communication, Titan, 30 Mar 2002). Phase I/II trials for treating **HIV** infection were planned for the 1st qtr of 2002 (not started as of Jun 2002) (Company Web Page, Titan, 25 Jan 2002; Direct communication, Titan, 18 Jun 2002).

Phase II In Phase I trials, po administration produced potentially therapeutic serum concentrations, with pharmacokinetics that indicated twice- or once-daily dosing. It was safe for up to 28 days (Press release, Titan, 20 Jul 2000; Direct communication, Titan, 30 Mar 2002).

#### Preclinical

Preclinical evaluation for use in treating **HIV** infection is underway (Direct communication, Titan, 18 Jun 2002). In vitro, **gallium** maltolate inhibited **ribonucleotide reductase** and enhanced the effects of nucleoside inhibitors such as didanosine and stavudine (both qv) (Company Web Page, Titan, 25 Jan 2002). Updated by SB on 24/6/2002.

DSTA World: Phase II Clinical Trial  
Canada: Phase II Clinical Trial  
United States: Phase II Clinical Trial

CC K6Z Anticancer, other  
J5A Antiviral, anti-HIV

CT Indication: Cancer, myeloma; Cancer, prostate; Cancer, bladder; Cancer, lymphoma, general; Infection, **HIV/AIDS**

ORGM CH-SY (Chemical synthesis, synthetic)

RTE A-PO (Alimentary, po)

RDAT 20000726 RNTE ##Act##New Product  
20000726 ##Act##New Chemical Structure New  
20001121 ##Act##New Indication Cancer, lymphoma and myeloma and **HIV/AIDS**

20010402        ##Act##Status changed Phase II Clinical Trial  
20020125        ##Est##New Indication Cancer, bladder and Cancer,  
lymphoma,

                  general

PHCD RIB-TP-AN; Enzyme, Oxidoreductase, Ribonucleoside triphosphate  
reductase inhibitor; Antineoplastic e.g. hydroxyurea;  
**Ribonucleotide reductase** inhibitor; E-OR-RIB-TP-AN;  
1.17.4.2.

PHCD E; E-AN; E-OR; E-OR-AN; E-OR-RIB; E-OR-RIB-AN; E-OR-RIB-TP;  
E-OR-RIB-TP-AN; OR; OR-AN; OR-RIB; OR-RIB-AN; OR-RIB-TP;  
OR-RIB-TP-AN; RIB; RIB-AN; RIB-TP; RIB-TP-AN; TP; TP-AN.

LN

Therapy (CC) | Pharmacology (PHCD) | Status (DSTC)

```
=====+=====+=====
K6Z      | RIB-TP-AN      | C2
-----+-----+-----
J5A      | RIB-TP-AN      | P
```

NRAT 6:Novelty Rating - Leading Compound

MRAT 3:Market Rating - US\$ 2001-5000 million

SRAT 4:Speed Rating - Faster than Average

TRAT 13:Total Rating - Total Rating

LCDAT 20020624: SB : Clinical information updated

STRUCTURE DIAGRAM IS NOT AVAILABLE

L31 ANSWER 188 OF 513 PROMT COPYRIGHT 2002 Gale Group

ACCESSION NUMBER: 2000:616469 PROMT  
TITLE: Titan Pharmaceuticals Acquires Novel Agent for the  
Treatment of Cancer and Viral Disease.  
SOURCE: Business Wire, (20 Jul 2000) pp. 245.  
PUBLISHER: Business Wire  
DOCUMENT TYPE: Newsletter  
LANGUAGE: English  
WORD COUNT: 576  
TEXT:

Business Editors

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--July 20, 2000

Titan Pharmaceuticals Inc. (AMEX: TTP) announced today that it has acquired worldwide rights to a novel, proprietary, experimental agent for the potential treatment of cancer and other conditions, including **HIV** infection. The product is an orally active agent that has completed initial Phase I clinical testing. Titan plans to begin Phase II clinical development in the treatment of certain cancers, and also evaluate its potential utility in other indications, including **HIV** infection.

The agent, **gallium** maltolate, contains an oral form of \*\*\*gallium\*\*\*, a semi-metallic element that is known to concentrate in malignant tumors and sites of infection. In previous pilot clinical studies, intravenously administered **gallium** has demonstrated preliminary evidence of anti-tumor activity in several cancer indications, including multiple myeloma, lymphoma and bladder cancer. Recent in vitro data indicate that **gallium** may also have potential for the treatment of **HIV** infection.

Titan believes **gallium** maltolate may unlock the therapeutic potential of **gallium**, by providing a unique orally active formulation for treatment of cancer and other diseases. Recent Phase I studies of \*\*\*gallium\*\*\* maltolate have demonstrated a good safety profile, with attainment of potentially therapeutic serum drug levels, and pharmacokinetics that support twice a day or once a day dosing.

Dr. Christopher Chitambar, Professor of Medicine at the Medical College of Wisconsin stated, "Previous clinical studies of intravenous **gallium** have shown promise in the treatment of a number of cancers and cancer-related conditions. An orally bioavailable agent such as **gallium** maltolate offers numerous potential advantages, and could provide an important new component to the therapy of several types of cancer." Dr. Chitambar has extensive research and clinical experience with the therapeutic applications of novel compounds in the treatment of cancer.

"We are very pleased to acquire rights to this unique proprietary therapeutic agent," commented Dr. Louis R. Bucalo, Chairman, CEO and President of Titan. " \*\*\*Gallium\*\*\* maltolate may provide the best practical means for utilizing the novel anti-cancer activity of **gallium**, and we look forward to

initiating further clinical testing."

With the addition of this new agent, Titan now has nine products in development, with seven in clinical testing. Titan is acquiring the product through the acquisition of GeoMed, Inc. a privately held California company founded for development of the agent. The completion of the acquisition is subject to customary closing conditions.

Titan Pharmaceuticals, Inc. is a biopharmaceutical company developing proprietary therapeutics for the treatment of central nervous system disorders, cancer and other serious and life-threatening diseases.

The press release may contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Such statements include, but are not limited to, any statements relating to the Company's development program and any other statements that are not historical facts. Such statements involve risks and uncertainties, including, but not limited to, those risks and uncertainties relating to difficulties or delays in development, testing, regulatory approval, production and marketing of the Company's drug candidates, unexpected adverse side effects or inadequate therapeutic efficacy of the Company's drug candidates that could slow or prevent product markets, the uncertainty of patent protection for the Company's intellectual property or trade secrets and the Company's ability to obtain additional financing if necessary. Such statements are based on management's current expectations, but actual results may differ materially due to various factors, including those risks and uncertainties mentioned or referred to in this press release.

THIS IS THE FULL TEXT: COPYRIGHT 2000 Business Wire  
PRODUCT CODE: \*PC2831000 Biological Products  
CORPORATE NAME: \*Titan Pharmaceuticals Inc. (Ticker Symbol: TNP)  
INDUSTRY CLASS: \*BUS Business, General; BUSN Any type of business  
N. AM. IND. CLASS: \*325414 Biological Product (except Diagnostic)  
Manufacturing  
GEOGRAPHIC TERM: \*CC1USA United States  
FEATURES: LOB; COMPANY